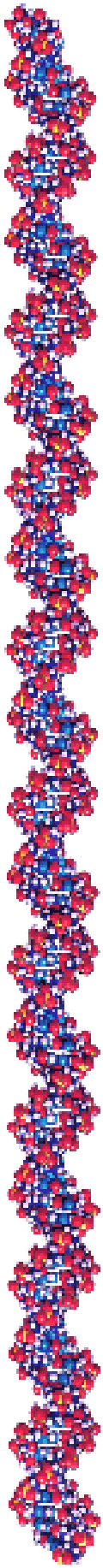


BIOTECHNOLOGY

Introduction

California is the birthplace of biotechnology, and today is home to 2,500 biotechnology companies. Combining engineering concepts with biological processes, biotechnology is used extensively in human medicine, but continues to find new applications in agriculture, manufacturing, and veterinary medicine. Biotechnology is used to improve plant and animal quality, process foods and assist environmental remediation.

The biotechnology industry is gaining momentum. Many California biotechnology companies have remarkable new therapies recently on the market, and encouraging developments in late-stage clinical drug trials. Amgen, in Thousand Oaks, markets a product to prevent infection in cancer patients. Amgen's neuroscience program is working on cures for Parkinson's disease. Genentech, in South San Francisco, markets a treatment for some forms of breast cancer, and is working on a bronchitis medication.

One of the most anticipated events in biotechnology was announced in June 2000. The Human Genome Project completed ahead of schedule a "working draft" of the sequence of genes that make up the human genetic blueprint. It is not possible to overstate the milestone this is for mankind.

Total companies	2,500
Public and private research institutions	75
Direct employment	212,700
Worldwide revenues	$20 billion
Exports	$4.2 billion
National Institute of Health grants awarded	$1.7 billion

Source: California Healthcare Institute

Compared to the U.S. biotechnology industry, California has a third of the public companies and 43 percent of the nation's employment. California public biotechnology companies generated half of the nation's total revenue, according to the 2000 study by Ernst & Young LLP.

Definition

Biotechnology relies on living organisms or biological systems. It uses organisms or their cellular components to reveal metabolic processes, produce a desired effect, or to make products that were formerly nonexistent, or rare and expensive. Biotechnology includes research into genetics and chemical processes that take a discovery and translate it into the relief of suffering. It can be used to modify the genetic structure of plants and animals to carry a desired trait to increase production or resist disease. Biotechnology includes the enzymes used in gas separation and purification, and the use of microscopic organisms to

clean up oil spills. The industry also includes the tools used to detect, measure and analyze biological components.

Biotechnology is not an industry in itself, but rather a composition of numerous high technology manufacturing and services industries. There is also no universally accepted set of industries that make up biotechnology. For the purposes of this report, biotechnology was defined using CorpTech, a commercial database of high technology companies.

The U.S. Bureau of the Census recently began replacing the Standard Industrial Classification (SIC) code with the North American Industry Classification System (NAICS). The NAICS is intended to coordinate industry definitions for tracking trade between the NAFTA nations of Canada, Mexico and the United States. The SIC was outdated, and could not accurately reflect the growing importance of the high technology industries of today. The table below shows the SIC codes and their corresponding NAICS. The NAICS is more detailed, and that is the reason there are sometimes several NAICS codes that correspond to one SIC code.

Product Examples	SIC	Industry	NAICS	New industry definition
Catalysts	2819	Industrial inorg. chem.	21112	Natural gas liquid extraction
Reagents			325998	Misc. chem'l products and preparation manu.
			331311	Alumina refining
			325131	Inorganic dye & pigment manufacture
			325188	All other basic inorganic chemical manu.
Drugs	2834	Pharmaceutical prep.	325412	Pharmaceutical preparation manufacture
Diagnostic agents	2835	Diagnostic substances	32514	Pharmaceutical prep.
Test kits			325413	In vitro diagnostic substances
Protein engineering	2836	Biological prods, ex. diag	325414	Biological products, except diagnostic
Enzyme technology	2869	Misc. organic chemicals	32511	Petrochemical manufacture
			325188	Other basic inorganic manufacture
			325193	Ethanol manufacture
			32512	Industrial gas manufacture
			325199	Other basic organic chemicals
Biotech equip.	3826	Lab analytical instruments	334516	Analytical lab instrument manufacture
Biotech services	8731	Comm. physical research	54171	R&D in physical, engineering & life sciences
	8734	Testing laboratories	54194	Veterinary services
			54138	Testing laboratories

History of Biotechnology

Researchers in California invented biotechnology in 1973 through a collaborative effort between the University of California, San Francisco and Stanford University, with funding by the National Institute of Health. The momentous event was the insertion of foreign, functioning genes into bacteria by recombinant DNA methods.

Research leadership translated into commercial leadership with the founding of the Cetus Corporation and Genentech in the Bay Area. Former employees from Genentech went on to form at least 18 other biotechnology companies. The first agricultural biotechnology company was ESCAgenetics Corp. of San Carlos.

Other "firsts" for California biotechnology include: the first recombinant pharmaceutical product (human insulin) approved for sale, by Genentech in 1982; the first polymerase chain reaction (PCR) performed by Cetus in 1985, winning a Nobel Prize for its discoverer, Dr. Kary Mullis; the first transgenic cow was born in 1990 to produce human milk proteins for making infant formula by GenPharm International, Inc.; and Amgen was the first biotechnology company to make the Fortune 500 in 1992.

The PCR developed by Cetus is now the primary method used for quickly multiplying copies of genetic material to create a sample that is large enough for analyzing the DNA within it. PCR is just one example of how a single biotechnology discovery finds applications in several diverse disciplines. It is also used in medical diagnostics to test for AIDS and pregnancy; and used by the judicial system to identify criminals, exonerate the innocent or establish paternity. It has found usage in anthropology on mummies and in tracing lineages in population genetics, as well as the genetic relationships between species.

Biotechnology Industry Clusters

Business clusters are attracted to a region based on the availability of capital, the transportation network, a favorable tax and regulatory structure, and the quality of life. In order to expand and flourish, businesses rely on the availability of human resources, technology and a networking infrastructure.

The state is heavily research-oriented with 75 public and private research institutions concentrating on human diagnostics, pharmaceuticals and therapeutic applications. The goal of research is the manufacture of products. The biotechnology industry therefore attracts a cluster of support firms composed of the researchers, entrepreneurs, suppliers, specialized law firms, venture capitalists and architects critical to the expansion of the industry. These clusters have been created in part by the leading-edge California biotechnology firms of Amgen, Affymetrix, Bio-Rad, Chiron and Genentech. In turn, these clusters generate and attract additional companies through spin-offs, mergers, out-of-state re-locations and new start-ups.

Cluster locations. The California Healthcare Institute identified seven biomedical clusters in the state: San Francisco Bay Area, Sacramento, Santa Barbara, Los Angeles, Inland Empire, Orange County and San Diego.

The San Francisco Bay area is the largest biotechnology cluster in the state with 645 companies and over 80,000 employees. The area is home to Stanford University and the University of California, Berkeley. The regions proximity to Silicon Valley promotes innovative combination of information technology and medicine.

The Los Angeles area is home to such world-famous research institutions as the University of California, Los Angeles, University of Southern California, and the California Institute of Technology. This is the second largest cluster with 35,400 employees in 467 firms.

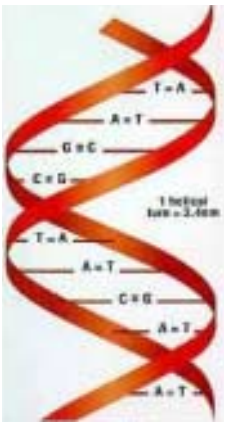
Orange County, San Diego, Santa Barbara and the Inland Empire add to Southern California's biotechnology industry with a total of 72,300 employees in 973 firms. The San Diego area is home to the Scripps Institute, the Salk Institute and the Burnham Institute.

The Sacramento region employs 4,600 in over 100 firms that are expanding primarily along Interstate 80. UC Davis provides research in agriculture and veterinary-related biotechnology. West of Davis, Vacaville is a growing center for biomedical manufacturing.

Residents in biotechnology clusters can enjoy significant benefits. One is the availability of leading edge medical treatments that are not yet available to the general population. Another is the multiplier effect of so many high wage jobs as a result of the income and spending of biotechnology employees. The jobs directly related to biotechnology result in the creation of many more jobs in the community.

California Biotechnology Products

Biotechnology products contribute to many important industries, including human and veterinary medicine, agriculture and food processing, industrial processes and environmental remediation. Each new discovery begets other new discoveries. The applications result in healthier lives, a cleaner environment, more efficient manufacturing, greater food production, and a better quality of life.



The Human Genome Project. Advances in biotechnology are expected to be made at a more rapid pace thanks to the Human Genome Project (HGP). The HGP is an international effort formally begun in 1990 to discover all the approximately 100,000 human genes, and to determine the complete sequence of the 3 billion DNA units. In the United States, the HGP is a joint effort funded by the Department of Energy and the National Institute of Health.

Each cell of an organism contains genes in the form of DNA. These are the "blueprints" for the structures and activities for the lifetime of every cell. The Human Genome Project seeks to identify the function and location of these genes by unraveling the DNA. The genetic data could help determine a diagnosis, or a course of treatment for illness or disease.

The HGP will increase the understanding of genetic material on a large scale, and play an increasingly important role in the diagnosis, monitoring and treatment of disease. There are long-anticipated ramifications for the pharmaceutical industry. By increasing the knowledge of biological processes, companies will be able to create "designer drugs" for specific applications geared to a specific individual.

Knowledge derived from the HGP creates the potential for using genes to treat disease by gene therapy. Genetic and acquired diseases could be treated through the replacement or supplementation of a defective gene, or to boost immunity to disease by adding a gene that suppresses tumor growth.

Genetic research is the basis of products made by Santa Clara-based Affymetrix. The company has introduced tiny glass chips, or microarrays, coated with DNA material. A few white blood cells or skins cells exposed to the DNA are all that is required for a rapid diagnosis for different types of cancer, genetic predispositions or infectious diseases. These "GeneChips" can be used to monitor a patient's response to treatment, make better matches for organ transplantation, and determine the efficacy of a particular drug. Some drugs may

have harmful side effects in the rare individual. But by testing a patient's response to a drug on a GeneChip, a drug that is most effective for the majority of patients can remain available.

Many advances in biotechnology are the result of the development of new high technology tools that were developed by such California companies as PE Biosystems, Affymetrix and Beckman Coulter. Advances in genomics, the identification and characterization of all the genes, would not have been as rapid without high throughput DNA sequencing. This allows the rapid screening of genetic material. Microarrays of thousands of genes reveal how the genes are expressed in the diseased state. Computer hardware and software products are used to mine the massive amounts of data generated for information about biological function. Computers also can screen thousands of compounds that might be used in potential new medicines.

Agriculture. California's agricultural industry uses diagnostic tests derived through biotechnology to detect animal and plant diseases. Food processors use biotechnology to diagnose food and feed contaminants.

California agriculture is the envy of the world. For over 50 years, California has been the number one agricultural state. Science and technology have long been keys to creating the marvel that is California agriculture. The state's own research and university extension programs have revolutionized many aspects of the state's agriculture. The University of California has, for instance, nearly 40 agricultural research centers and programs. In the Central Valley, two of the centers for agricultural research are the University of California, Davis and California State University, Fresno.

Today, biotechnology is providing major contributions to California's leadership in agricultural technology. Genetic improvements have led to higher-yielding varieties with improved pest resistance, better taste and longer shelf life for nuts, fruits and vegetables. Agricultural biotechnology research conducted in California helps to improve the lives of people all over the world. The knowledge gained in the development of higher yielding plants is used to aid poorer nations in creating more productive farmland, with crops of greater yield and increased nutrition.

The production of bioengineered agricultural products reduces the need for pesticides, thus reducing the negative impact on the environment from spraying and run-off. Nevertheless, there is a growing resistance to food products that have been genetically altered, particularly in Europe and Asia.

Biotechnology has produced hundreds of enzymes used in food processing and other manufacturing. Yeast is the living organism that has been used for centuries in the fermentation of beverages, and the making of bread. Biotechnology created the enzyme for the manufacture of some hard cheeses that is superior to that which naturally occurs in cows' stomachs.

Veterinary. Biotechnology has created pharmaceuticals for the prevention of illness and disease in animals. A recent innovation is "Revolution", a once-a-month topical application for the all-in-one prevention of heartworm, fleas, ticks, mites, mange, and intestinal parasites in dogs. There are now also therapeutic drugs available for animals that suffer anxiety as a result of being separated from their owners all day.

Biotechnology has created veterinary medicines that are helping geriatric zoo animals live more comfortable lives. Due to their unnaturally long lives, some zoo animals are experiencing arthritis, kidney problems, heart problems, and other age-related afflictions.

Bioremediation. Microorganisms are used in wastewater treatment and in the cleanup of oil spills and hazardous waste. Enzymes in wastewater improve the efficiency and performance of the treatment process by stimulating the existing microbes into creating a balanced growth environment. Oil spills as small as the driveway and as large as one from an oil tanker can be cleaned up with naturally occurring bacteria that destroy waste oil and grease. These products are finding use in maritime situations to clean heavy equipment, decks and the oily bilge water. On hazardous waste spills, enzymes convert heavy metals into safe by-products that can safely enter the water supply.

Infrastructure

The California biotechnology industry enjoys an infrastructure not duplicated anywhere else. The state offers top incentives to the industry, an environment supportive of the entrepreneur, and world-renowned research facilities. The state also has leading-edge electronics, and offers a skilled labor force. There is an excellent transportation system by sea, land and air, and a ready-made market of 34 million in its own backyard.

Research resources. All scientific advancements begin with research. And California universities and research institutes have played a major role in developing successful biotechnology companies. These include the nine-campus University of California, Stanford University, University of Southern California, California Institute of Technology, as well as many private research facilities.

A survey by the California Healthcare Institute (CHI) showed that a California research university or institution played a central role in the growth of 28 percent of the biotechnology firms surveyed. Forty-six percent have a clinical research or sponsored research agreement, and 31 percent have a patent license agreement with a California public or private health/academic institution.

A University of California study showed that 1 in 4 California biotechnology firms was founded by a University of California (UC) scientist, 6 of the 10 top selling biotechnology pharmaceuticals stem from UC research, and 85 percent of California biotechnology firms employ UC alumni.

Building upon those successes, UC has initiated BioSTAR, a program to build research linkages between California businesses and UC scientists in the area of biotechnology. UC San Francisco has begun construction on a molecular research complex at Mission Bay.

This complex will allow scientists, graduate students and staff to both work and live on the campus. Surrounding the campus, five million square feet of research, office, manufacturing and multimedia space will be rented out to commercial biotechnology tenants in a deliberate model of the Stanford Industrial Park, the nucleus of Silicon Valley.

Stanford University received a $150 million gift from the founder of Silicon Graphics Inc., resulting in the creation of the Stanford Bio-X program. The program is an effort to bring together interdisciplinary research in biotechnology and biomedicine. The gift helped to fund a supercomputer with the computational power required to unravel the genetic code as it is revealed by the Human Genome Project.

Research and training are essential for biotechnology companies. Typically, a biotechnology company invests 42 percent of its operating expenditures on research and development. Large pharmaceutical companies are major investors. One example is Switzerland-based Novartis. Novartis bought nearly half an interest in Chiron Corporation, based in Emeryville, and owns SyStemix, Inc. in Palo Alto. Novartis added to the roster of research firms in San Diego with the foundation of two new research facilities. The Novartis Agricultural Discovery Institute will emphasize protection of health and the environment through agricultural research. In La Jolla, the Novartis Institute of Functional Genomics will employ the growing knowledge of how genes function in disease, and apply it to human therapeutics.

Investment. These novel and breathtaking biomedical advances disclose again why international investors and the world scientific community gravitate to California for developing major breakthroughs in medicine and biopharmaceutical therapies.

Researchers in San Francisco invented biotechnology in 1973. Since that time, new technologies and new tools have continued to generate innovative companies. Both federal and state government have been constant investors in this industry.

To further encourage biotechnology, the State of California has the highest research and development tax credit in the nation. Companies are allowed a credit of 12 percent for qualifying research expenses (research done in house), and 24 percent for basic research payments (payments to an outside company).

Federal investment is partly evidenced by the $1.7 billion in grant awards to California biotechnology research, the largest amount in the nation. The world's largest system of government laboratories is in the United States. The research conducted at these labs accounts for 14 percent of total U.S. research and development.

Two federal laboratories in California are involved with the genome project, among other things. In Livermore, the Lawrence Livermore National Laboratory, in conjunction with the Los Alamos National Laboratory in New Mexico, contributed to the description of the genetic mechanism that contributes to the onset of at least nine diseases, including Huntington's disease. The Lawrence Berkeley National Laboratory in Berkeley has produced two megabases of human gene sequences that led to insights into the many immune responses thought to be involved in autoimmune diseases.

Venture Capital. The biotechnology industry is highly regulated by the federal government. As a result of stringent requirements, biotechnology innovations are expensive and come only after a lengthy process. Of 5,000 potential new medicines, only one will reach the pharmacy shelf after 12 to 15 years, and an average of $500 million.

Clinical Trials

	Preclinical Testing	Phase I	Phase II	Phase III	FDA	Phase IV
Years	3.5	1	2	3	2.5	Additional Post marketing testing required by FDA
Test Population	Laboratory and animal studies	20 to 80 healthy volunteers	100 to 300 patient volunteers	1000 to 3000 patient volunteers	Review process / Approval	
Success Rate	5,000 compounds evaluated	5 compounds enter trials			1 compound is approved	

Following preclinical testing, an application is filed for an investigational new drug, describing how the compound is thought to work in the body. After the three clinical phases, an application is filed for a new drug. This application includes all the scientific information gathered by the company. Though this is the most rigorous drug approval process in the world, the potential gain is so high for blockbuster drugs such as Claritin, Viagra and Prozac that investors continue to show their confidence in the long-term prospects of biotechnology.

In 2000, $1.2 billion of venture capital was invested in California biotechnology companies, more than twice the amount invested in 1999. The first quarter of 2001 was off to a very strong start, with $448 million invested. More than half the 2001 investment was made in companies in the San Diego area. The San Francisco Bay region was the next largest recipient.

Biotechnology is increasingly an international endeavor. Today, there are exceptional opportunities for foreign direct investment through long-term financing of basic research, joint ventures, the establishment of new subsidiaries or the purchase of equity interests. Since 1991, foreign direct investment into California drug companies increased more than 50 percent. Biotechnology companies need the long-term, stable sources of capital. In exchange, foreign investors have access to the latest technology.

Electronics. The biotechnology industry benefits from the proximity to the state's world famous electronics industry. Electronics are playing an ever-expanding role in the biotechnology industry, with hardware that speeds the analyses of far more samples, and software to help analyze the mounds of data generated.

Like most high-technology companies, biotechnology companies devote an above-average portion of their resources to research. The biotechnology industry benefits from proximity to Silicon Valley's leading edge electronics that have greatly accelerated the rate of research. For example, computer-generated molecular models increased the rate at which possible drugs can be tested, thereby decreasing the time it takes to get FDA approval.

As in nearly every other industry, the Internet plays an important role. The Internet allows the rapid exchange of ideas, and the timely posting of experimental results without having to wait for formal presentations. The data storage capabilities of the Internet have been a boon to the Human Genome Project where the databases are available for review 24 hours a day, every day.

Skilled labor force. California has a highly skilled labor force. Nearly a quarter of adults have college degrees. There are nine University of California campuses, 22 California State University campuses and 106 community colleges. Approximately 13,000 students graduate annually from the UC and CSU systems in the fields of biological life sciences, physical sciences and health professions. In addition, those already in the industry may enhance their existing skills and knowledge by taking additional courses.

California has 213,000 employed directly in biotechnology firms. Of these, nearly a quarter are involved in biotechnology research at one of the state's federal facilities, private research institutes or major universities. California has nearly a fifth of the nation's employment in physical research labs, and leads the nation in the number of Nobel Prize winners. The University of California boasts 20 Nobel laureates and 300 members of the National Academy of Sciences among its faculty. The Stanford University faculty has 15 Nobel laureates and 126 members of the National Academy of Sciences.

Market. California has the largest population in the nation, with a built-in market of 34 million people. As with the rest of the nation, and most other developed nations, it is an aging population. The population and its political institutions have long supported leading-edge medical research.

California is strategically located to market biotechnology products. The state has six seaports, including one of the largest seaports in the world at Los Angeles-Long Beach. California products are shipped all around the Pacific Rim. Its proximity to the NAFTA nations of Mexico and Canada ensures ready access to these growing markets. For the first time, Mexico was the top ranked destination for California exports in 1999. Canada ranked third after Japan.

The state offers 9 international and domestic hub airports, as well as 314 public airports. And from distribution centers in the Central Valley, overnight deliveries can be made anywhere in the state.